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EXAMINER: STANTON, B

ART UNIT: 1804 | PAPER NUMBER: 6

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DATE MAILED: 04/30/96

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

☑ This application has been examined ☑ Responsive to communication filed on 2/8/96 ☐ This action is made final.

A shortened statutory period for response to this action is set to expire THREE (3) month(s), 0 days from the date of this letter. Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☐ Notice of References Cited by Examiner, PTO-892.
2. ☐ Notice of Draftsman's Patent Drawing Review, PTO-948.
3. ☑ Notice of Art Cited by Applicant, PTO-1449.
4. ☐ Notice of Informal Patent Application, PTO-152.
5. ☐ Information on How to Effect Drawing Changes, PTO-1474.
6. ☐ _____

Part II SUMMARY OF ACTION

1. ☑ Claims 10, 60-111 are pending in the application.
   Of the above, claims 10, 63-66, AND 103 are withdrawn from consideration.
2. ☐ Claims _____ have been cancelled.
3. ☐ Claims _____ are allowed.
4. ☑ Claims 60-62, 67-102, AND 104-111 are rejected.
5. ☐ Claims _____ are objected to.
6. ☐ Claims _____ are subject to restriction or election requirement.
7. ☐ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.
8. ☐ Formal drawings are required in response to this Office action.
9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable; ☐ not acceptable (see explanation or Notice of Draftsman's Patent Drawing Review, PTO-948).
10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____. has (have) been ☐ approved by the examiner; ☐ disapproved by the examiner (see explanation).
11. ☐ The proposed drawing correction, filed _____, has been ☐ approved; ☐ disapproved (see explanation).
12. ☐ Acknowledgement is made of the claim for priority under 35 U.S.C. 119. The certified copy has ☐ been received ☐ not been received ☐ been filed in parent application, serial no. _____; filed on _____.
13. ☐ Since this application apppears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.
14. ☐ Other

The instant application is a continuation of Application Serial No. 07/950,356, filed 9/24/92, now abandoned, which is a continuation of Application Serial No. 07/269,926, filed 11/10/88, now U.S. Patent No. 5,192,553, which is a continuation-in-part of Application Serial No. 07/119,746, filed 11/12/87, now U.S. Patent No. 5,004,681.

Applicant is advised that references have been stricken from the form PTO-1449 submitted on 2/8/96. Those references marked with an asterisk (*) have been stricken because they are duplicative of other citations. Those references marked with a double dagger have been stricken because no copy was provided and these references were not of record in the parent applications to the instant Application.

Claims 10 and 60-111 are pending in the instant Application.

The Response to Restriction requirement filed 2/8/96 (Paper No. 5) has been entered.

Applicant's election with traverse of the invention of Group II, claims 60-62, 67-103, and 105-111 in Paper No. 5 is acknowledged. The traversal is on the ground(s) that the individual groups of claims are not distinct invention, but rather represent a web of knowledge which merit examination in a single application. Applicant also argues that no burden of search exists for examination of the several invention outlined in the restriction requirement mailed 9/14/95 (Paper No. 4). These arguments are not found persuasive because the standard of restriction is based upon the obviousness of one invention over another (i.e. patentable distinctness) and whether or not a burden of search exists for each invention. While inventions may be related, if they are drawn to separate inventions each of which requires a non-coextensive area of search and corresponding considerations then restriction is proper. In the instant case and for reasons set forth in the restriction requirement mailed (Paper No. 4), such a burden of search is found to exist. Applicant has offered no evidence that the searches required for the several inventions would be coextensive or that the several inventions would have been obvious, one over the other.

The requirement is still deemed proper and is therefore made FINAL.

In Paper No. 5, applicant has indicated that in the groupings of inventions set forth in Paper No. 4, an misnumbering error was made such that claim 103, rather than claim 104 was included in the invention of group II. The examiner appreciates applicant pointing out this error. The restriction

requirement as advanced in Paper No. 4 is modified as hereinbelow to account for the correctly numbered claims.

Restriction to one of the following inventions is required under 35 U.S.C. § 121:

I. Claim 10, drawn to recombinant cells, classified in Class 435, subclass 240.2.

II. Claims 60-62, 67-102, and 104-111, drawn to treatment methods wherein blood is directly administered, classified in Class 424, subclass 529.

III. Claims 63-65, drawn to treatment methods wherein blood cells are grown *in vitro* prior to administration, classified in Class 435, subclass 240.21 and Class 424, subclass 529.

IV. Claim 66 and 103, drawn to treatment methods wherein recombinant cells lines are prepared and used, classified in Class 514, subclass 44 and Class 424, subclass 529..

I. Claims 10, 63-66, and 103 are withdrawn from further consideration by the examiner, 37 C.F.R. § 1.142(b), as being drawn to a non-elected invention, the requirement having been traversed in Paper No. 5.

Claims 60-62, 67-102, and 104-111 are currently under examination.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The specification is objected to under 35 U.S.C. § 112, first paragraph, as failing to provide an enabling disclosure.

The invention as defined by pending claims 82-102, is drawn to treatment methods wherein hematopoietic stem cells are administered to a host. However, the specification fails to provide an enabling disclosure for such methods because it fails to provide teachings regarding what such a stem cell would comprise and how one would have obtained and utilized such cells. The term "stem cell" is a generic designation used in the differentiation art to indicate that a given cell is capable of giving rise to a divergent group of progeny cells with variant phenotypic properties. A continuing research effort is aimed at identifying and isolating an "ultimate stem cell" that is capable of giving rise to all of the divergent cell types of the hematopoietic system. The instant specification details the analysis of

hematopoietic precursor cells in Section 6.6 and its associated subsections. Said analyses include methods for the identification of CFU-GM, BFU-E and CFU-GEMM progenitor cells (see section 6.6 beginning on page 83). No guidance is present in the specification for the identification, characterization of isolation of any "ultimate" stem cell. However, guidance is present that indicates which groups of cells that may be isolated from whole blood would be useful in the method of the instant invention (see e.g. section 6.3 and associated subsections beginning on page 75). Since the identification of ultimate stem cells is an ongoing field of research and no established guidelines are present in the art for such and further since in the absence of suitable guidance the practitioner would have been required to have exercised undue experimentation in the practice of the claimed invention as currently claimed. Applicant is advised that as pending, the specification fails to provide an enabling disclosure for the invention as claimed. However, should limitation of the extent of the instant invention to utilization of particular enriched fractions of blood which include identifiable and assayable populations of cells would obviate the instant grounds of objection and corresponding rejection of the claims.

Claims 82-102 are rejected under 35 U.S.C. § 112, first paragraph, for the reasons set forth in the objection to the specification.

Claims 60-62, 67-102 and 104-111 are rejected under 35 U.S.C. § 103 as being unpatentable over Nakahata et al., 1982 (DX), Saunders, 1965 (AN) and either of Ende, 1966 (BV) or Ende et al., 1972 (BU), the preceding combination in view of Applicant's admissions on pages 10, 11, 27 and 28, Herzig et al., 1983 (CQ), McGlave et al., 1985 (DT) and Fabian et al., 1982 (BW).

The instant invention is directed towards methods of treating diseases involving depletion of hematopoietic cells by administration of cyropreserved neonatal or fetal blood cells to a patient.

Each of Ende (BV) and Ende (BU) teaches the treatment of patients with human fetal (cord) blood. In the case of Ende (BV), the patient suffered from leukopenia and general anemia and was treated with human umbilical cord blood (see e.g. Table I, page 81). In the case of Ende (BU) the patient suffered anemia due to conventional antileukemic therapy (see e.g. introduction on page 276). Neither of Ende (BV) or Ende (BU) teaches the cryopreservation of fetal cord blood or the treatment of the variety of anemic disorders as instantly claimed.

Nakahata teaches that human fetal cord blood is comprised of a variety of hematopoietic progenitor cells that are similar in composition to those present in adult bone marrow (see e.g. Table I, page 1326).

Each of Herzig and McGlave teach the utilization of bone marrow transplantation (BMT) for the treatment of disorders associated with anemia. Herzig specifically discloses the use of BMT and that bone marrow contains a variety of hematopoietic precursor cells (see e.g. section entitled Viability beginning on page 125). Herzig also teaches the use of cryopreserved bone marrow in therapeutic applications (see e.g. section entitled Cryopreservation beginning on page 126). McGlave discloses both allogeneic and autologous BMT for treatment of a variety of disorders (see e.g. section entitled Clinical Applications of Bone Marrow Transplantation, beginning on page 171).

Fabian and Saunders disclose cryopreservation of multipotential hematopoietic cells (see e.g. Fabian; Abstract and Table I on page 121 and Saunders; column 2, lines 46-62). Saunders additionally discloses the use of mannitol as a cryoprotectant that may be administered concomitantly with cryopreserved blood.

Applicant's admit within the body of the paragraph bridging pages 10 and 11 that bone marrow has been used with increasing success for treatment of a variety of disorders and further admit on page 27 that it was known that human cord blood contains a high proportion of hematopoietic precursor cells.

As indicated above, human cord blood and bone marrow cells have similar properties in that they both comprise significant populations of hematopoietic progenitor cells. Therefore, since the cellular components of these two compositions were known to be similar, one would have had a reasonable expectation of success in utilizing cord blood and its components in situations where bone marrow cells were employed. It was recognized that cryopreservation was a useful method for preserving cells prior to administration and additionally Saunders explicitly noted that certain cryoprotectants could be co-administered with blood without inducing adverse effects. Thus, it would have been obvious to one or ordinary skill in the art at the time the invention was made to have utilized cryopreserved cord blood cells in methods of treating any disorder in which the use of bone marrow cells would have been appropriate.

One would have been motivated to use fetal blood cells in a treatment method because it was recognized that such cells contained high proportions of hematopoietic progenitor cells which the artisan would have recognized as useful in the treatment of a variety of disorders characterized by anemia. One would have used cryopreserved blood cells because one would have expected that by preserving blood, one would have increased the storage life of blood to be used in future applications.

In regard to claims 82-102, it is noted that the instant grounds of rejections is applicable in so far as said claims could be considered to comprise the use of hematopoietic precursor cells rather than the use of the ultimate hematopoietic stem cell.

Therefore, for the preceding reasons, the claimed invention would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Claim 60-62, 67-102 and 104-111 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 13-35, 47-53 and 57 of U.S. Patent No. 5,192,553. Although the conflicting claims are not identical, they are not patentably distinct from each other because the generic claims of the instant invention encompass the claims of the '553 patent and as such are obvious over the patented species claims.

The obviousness-type double patenting rejection is a judicially established doctrine based upon public policy and is primarily intended to prevent prolongation of the patent term by prohibiting claims in a second patent not patentably distinct from claims in a first patent. *In re Vogel*, 164 USPQ 619 (CCPA 1970). A timely filed terminal disclaimer in compliance with 37 C.F.R. § 1.321(b) would overcome an actual or provisional rejection on this ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 C.F.R. § 1.78(d).

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian R. Stanton whose telephone number is (703) 308-2801. The examiner can normally be reached on Monday through Thursday from 6:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jacqueline Stone can be reached on (703) 308-3153. The fax phone number for this Group is (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-1096.

Brian R. Stanton

BRIAN R. STANTON
PATENT EXAMINER
GROUP 1800

Brian R. Stanton, Ph.D.
30 April 1996